PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In re Application of	)	
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Michael A. Innis, *et al.*	)	Examiner: David S. Romeo
	)	
Serial No. 09/639,273	)	Group Art Unit: 1647
	)	
Filed: August 15, 2000	)	Atty. Dkt. No. 012441.00002

For: **Production of Tissue Factor Pathway Inhibitor**

RESPONSE TO RESTRICTION REQUIREMENT

The Honorable Assistant Commissioner for
Patents
Washington, D.C. 20231

Sir:

In response to the Restriction Requirement mailed December 6, 2001, Applicants request consideration of the following remarks. It is believed that no fees are required for consideration of this response. If any fees are required, please charge our deposit account no. 19-0733.

Applicants respectfully traverse the requirement for restriction. If the restriction requirement is maintained, Applicants elect Group VII for prosecution on the merits.[1]

The currently pending claims 1-11 are the same claims as originally filed in the parent application, Ser. No. 08/854,764, which issued as U.S. Patent 6,103,500. The restriction requirement of the parent application (paper no. 5, mailed Nov. 22, 1995) placed claims 1-6 and

[1] Applicants also traverse the requirement for election of one of the species listed in claim 6 (yeast genotypes). Claim 6 was previously examined in the parent application. However, should this requirement be maintained, Applicants elect the AB122 genotype.

8-10 together as a first group and claims 7 and 11 as a second group. The present restriction of the same 11 claims has resulted in nine groups instead of two. Claims 1-6 and 8-10 were previously examined in the parent application and have already issued with some amendments. Thus, this response will focus on previously non-elected claims 7 and 11.

The present restriction has placed claim 7 as directed to TFPI into Group VII, claim 7 as directed to TFPI-2 into Group VIII, and claim 11 into Group IX. Because the Office Action fails to provide an appropriate justification for restriction, Applicants respectfully request that claims 7 and 11 be examined as a single group.

Claim 7 is directed to factor VIIa/TF/Xa binding protein prepared by the method of claim 1. Claim 11 is directed to factor VIIa/TF/Xa binding protein prepared by the method of claim 10, which recites the method of claim 1 wherein the factor VIIa/TF/Xa binding protein is a mutein of TFPI having arginine in the P1 reactive site of Kunitz-type domain 1. Claims 7 and 11 were considered as a single group in the restriction requirement of the parent application. The restriction requirement of the parent application had mistakenly placed claim 7 initially into the same group as claims 1-6 and 8-10. However, the subsequent office action (paper no. 7, mailed Feb. 16, 1996) stated "Claim 7 should have been grouped with claim 11, which is also drawn to a product produced by the method." Paper No. 7 of Ser. No. 08/854,764 at page 2, last paragraph.

Claims 7 and 11 are both directed to TFPI or related proteins produced by essentially the same process. The primary difference between the claimed proteins is found in their sequence, which requires that the first step of incubating yeast cells with a replicable cloning vehicle be carried out using a different nucleotide sequence. In claim 7, the cloning vehicle comprises a nucleotide sequence encoding a factor VIIa/TF/Xa binding protein. Claim 11 additionally

requires that the encoded factor VIIa/TF/Xa binding protein be a mutein of TFPI having an arginine in the P1 reactive site of Kunitz-type domain 1.

Muteins of TFPI as encompassed by claim 11 are described in the specification *inter alia* at page 9, lines 11-21:

> Muteins of TFPI or TFPI-2 may also be prepared according to the method of the invention. Muteins within the scope of this definition include: (a) TFPI or TFPI-2 muteins having 1-5 conservative amino acid substitutions that do not substantially change the conformation of the molecule; (b) TFPI or TFPI-2 muteins with amino acid substitutions that eliminate one or more of the sites for N-linked glycosylation; (c) TFPI muteins having 1-5 amino acid substitutions that change a residue of TFPI to a corresponding residue of TFPI-2; (d) TFPI-2 muteins having 1-5 amino acid substitutions that change a residue of TFPI-2 to a corresponding residue of TFPI; (e) TFPI or TFPI-2 muteins with amino acid substitutions in P1 reactive sites in one or more Kunitz-type domains; and (f) TFPI or TFPI-2 muteins with amino acid substitutions at positions within 5 amino acids of the P1-reactive sites in one or more Kunitz-type domains.

The TFPI muteins recited in claim 11 differ from TFPI by only a small number of amino acids as described above. Thus, consideration of claims 7 and 11 as a single group would not present an unusual burden for the examiner, because the recited sequences would share a major portion of identical amino acids, and related protein sequence variants are commonly recited by even a single claim. Furthermore, according to the present restriction requirement the subject matter of Groups VII-IX all fall within the same class and subclass.

For the reasons discussed above, Applicants request that claims 7 and 11 be examined as a single group. If such a restriction is permitted, Applicants elect claims 7 and 11 for prosecution on the merits in this application.

Respectfully submitted,

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